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EXAMINER	
MYERS, CARLA J	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 07/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/697,013	STANTON, VINCENT P.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-58* is/are pending in the application.

4a) Of the above claim(s) *17-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *57 and 58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the amendment filed May 3, 2004. Applicants arguments have been fully considered but are not persuasive to overcome all grounds of rejection. All rejections not reiterated herein are hereby withdrawn. This action is made final.

Claims 1-16 have been canceled. Claims 17-58 are pending. Claims 17-56 are withdrawn from consideration as being drawn to an invention non-elected without traverse in the response of September 5, 2003.

Specification

2. The disclosure is objected to because of the following informalities:

The specification is objected to because the assigned SEQ ID NOs have not been used to identify each sequence listed, as required under 37 CFR §1.821(d). In particular, the sequence set forth in Table 2 should be accompanied by the appropriate sequence identifier (i.e., nucleotides 14701-37680 of SEQ ID NO: 5). Additionally, the description of figures 34 and 35 should include the sequence identifier for the sequences set forth in these figures or the figures themselves should be amended to include the sequence identifiers.

It is noted that in the response filed May 3, 2004, Applicants did not specifically address the above objection. Accordingly, the objection is maintained for the reasons stated above.

THE FOLLOWING GROUNDS OF REJECTION HAVE BEEN MODIFIED IN VIEW OF THE AMENDMENTS TO THE CLAIMS:

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Definitions: [from UTILITY GUIDELINES TRAINING MATERIALS; repeated from http://www.uspto.gov/web/menu/utility.pdf]

"Credible Utility" - Where an applicant has specifically asserted that an invention has a particular utility, that assertion cannot simply be dismissed by Office personnel as being "wrong". Rather, Office personnel must determine if the assertion of utility is credible (i.e., whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided). An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based is inconsistent with the logic underlying the assertion. Credibility as used in this context refers to the reliability of the statement based on the logic and facts that are offered by the applicant to support the assertion of utility. A *credible* utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for such use. For example, no perpetual motion machines would be considered to be currently available. However, nucleic acids could be used as probes, chromosome markers, or forensic or diagnostic markers. Therefore, the credibility of such an assertion would not be questioned, although such a use might fail the *specific* and *substantial* tests (see below).

"Specific Utility" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be *specific* in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

"Substantial utility" - a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic

method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.

B. A method of treating an unspecified disease or condition. (Note, this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C. 101.)

C. A Method of assaying for or identifying a material that itself has no "specific and/or substantial utility".

D. A method of making a material that itself has no specific, substantial, and credible utility.

E. A claim to an intermediate product for use in making a final product that has no specific, substantial, and credible utility.

Note that "throw away" utilities do not meet the tests for a *specific* or *substantial* utility. For example, using transgenic mice as snake food is a utility that is neither specific (all mice could function as snake food) nor substantial (using a mouse costing tens of thousands of dollars to produce as snake food is not a "real world" context of use). Similarly, use of any protein as an animal food supplement or a shampoo ingredient are "throw away" utilities that would not pass muster as specific or substantial utilities under 35 U.S.C. ' 101. This analysis should, or course, be tempered by consideration of the context and nature of the invention. For example, it a transgenic mouse was generated with the specific provision of an enhanced nutrient profile, and disclosed for use as an animal food, then the test for specific and substantial *asserted* utility would be considered to be met.

"Well established utility" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in

the art. "Well established utility" does not encompass any "throw away" utility that one can dream up for an invention or a nonspecific utility that would apply to virtually every member of a general class of materials, such as proteins or DNA. If this is the case, any product or apparatus, including perpetual motion machines, would have a "well established utility" as landfill, an amusement device, a toy, or a paper weight; any carbon containing molecule would have a "well established utility" as a fuel since it can be burned; any protein would have well established utility as a protein supplement for animal food. This is not the intention of the statute.
See also the MPEP at 2107 - 2107.02.

4. Claims 57 and 58 are rejected under 35 U.S.C. 101 because the claimed invention lacks a credible, substantial, specific or well-established utility.

The claims are drawn to methods for determining whether an individual has a variant nucleotide at a polymorphic site in the ApoE gene wherein the polymorphic site is at position 16541, 16747, 16965, 17030, 17387, 17785, 17937, 18476, 19311, 20234, 21349, 23524, 23707, 232759 and 23805 of SEQ ID NO: 5.

The claimed methods are not supported by either a specific and substantial asserted utility or a well-established utility. The specification fails to provide objective evidence of any activity for the claimed nucleic acids containing polymorphisms and thereby any utility for the methods for detecting said polymorphisms. The specification (page 19) states that the claimed methods can be used for detecting genotypes or haplotypes as indicative of risk of a disease or condition, such as coronary heart disease, non-Alzheimer's neurological disease, Alzheimer's disease, stroke, or brain trauma. However, the specification has not established that the stated polymorphisms in the human ApoE gene are associated with any particular disease or condition. The specification provides information regarding the frequency of the polymorphisms

in the population, but has not established that any of the polymorphisms are associated with a particular activity or condition in any specific population. The specification indicates that the genotypes can be used for selecting treatment for a disease or for determining the prognosis of a disease. However, the specification has not established a nexus between any disorders and any of the polymorphisms set forth in claim 2. The specification (page 20) further suggests that polymorphisms can be used to identify an individual. However, such a utility is general because it is a property of all polymorphisms and thereby is not considered to be a specific utility. The specification (page 21) also states that the polymorphisms can be used to determine whether a haplotypes is associated with a disease risk. It is stated that such a method would require determining ApoE haplotypes for each individual in a set of individuals, dividing the set of individuals into at least two groups based on ApoE haplotypes and determining whether individuals in a group differ from individuals having a different ApoE haplotypes with respect to incidence, prevalence, severity, or progression of disease. However, such a utility is not considered to be substantial because it essentially involves performing research in order to find a utility for the polymorphisms, i.e., in order to establish that the polymorphisms are associated with disease.

As stated in Brenner v. Manson, 383 U.S. 519 535-536, 148 USPQ 689, 696 (1966) " a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion". Support for an asserted utility that is specific and substantial would require, for example, a showing of a particular function for the ApoE polymorphisms, or a showing of a clear correlation between the disclosed polymorphisms and the occurrence of disease or an alteration in response to drug treatment. Merely identifying and studying

the properties of the polymorphisms or performing assays to determine a correlation between the polymorphisms and disease does not constitute a "real world" context of use. Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility has not been assessed. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the nucleic acid compounds such that another non-asserted utility would be well established for the compounds. Accordingly, the claimed invention is not supported by either a specific or substantial asserted utility or a well-established utility. Applicant is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 57 and 58 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Furthermore, the specification has not taught one of skill in the art how to use each of the polymorphisms and thereby has not taught one of skill in the art how to use the methods of determining whether an individual has a variant

nucleotide at a polymorphic site at positions 16541, 16747, 16965, 17030, 17098, 17387, 17785, 17937, 18476, 19311, 20234, 21349, 23524, 23707, 23759, 23805, and 37237 of SEQ ID NO: 5. The specification (page 19) states that the claimed methods can be used for detecting genotypes or haplotypes as indicative of risk of a disease or condition, such as coronary heart disease, non-Alzheimer's neurological disease, Alzheimer's disease, stroke, or brain trauma. However, the specification has not established that the polymorphisms set forth above are in fact associated with any particular disease or condition. The specification provides information regarding the frequency of the polymorphisms in the population, but has not established that any of the polymorphisms are associated with a particular activity or condition in any specific population. The specification indicates that the genotypes can be used for selecting treatment for a disease or for determining the prognosis of a disease. However, the specification has not established a nexus between any disorders and any of the stated polymorphisms. The specification (page 20) further suggests that methods for determining a genotype by detecting a polymorphism can be used to identify an individual. However, such a use is considered to require additional experimentation because the specification has not established that any one particular polymorphism is correlated in a specific manner with a population of individuals and can be used in a predictable manner to identify an individual. The specification (page 21) also states that the polymorphisms can be used to determine whether a haplotype is associated with a disease risk. It is stated that such a method would require determining ApoE haplotypes for each individual in

a set of individuals, dividing the set of individuals into at least two groups based on ApoE halotypes and determining whether individuals in a group differ from individuals having a different ApoE haplotypes with respect to incidence, prevalence, severity, or progression of disease. Accordingly, such a method would require extensive experimentation.

In view of the lack of specific teachings provided in the specification as to an association between the ApoE polymorphisms and any particular disease or response to therapy, undue experimentation would be required for one of skill in the art to practice the invention as it is broadly claimed.

RESPONSE TO ARGUMENTS:

In the response filed May 3, 2004, Applicant's traversed the 101 and 112 rejections by stating that the specification discloses specific polymorphisms in the ApoE gene. It is asserted that one can determine if these polymorphisms are associated with a disease risk or response to therapy and thereby detecting the presence of the claimed polymorphisms provides a specific and substantial utility.

Applicant's arguments have been fully considered but are not persuasive. Applicant's have not disclosed a specific and substantial utility for the claimed polymorphisms and methods of detecting the polymorphisms. Rather, Applicant's have provided only the methodology of how to go about searching for a utility for the ApoE polymorphisms. Applicant's state that the polymorphisms can be analyzed to determine which, if any, of these polymorphisms is associated with one or more of a variety of diseases or with a response to an unstated type of therapy. However, the use of a nucleic acid containing a polymorphism for

scientific inquiry does not constitute a meaningful utility. 35 U.S.C. § 101 requires a utility that is substantial – i.e., a utility that provides a specific benefit to the public in a currently available form. Brenner, 383 U.S. at 534-35, 148USPQ at 695. The use of a nucleic acid as a research tool does not provide a specific benefit to the public in a currently available form. Further, the specification has not established that any of the claimed polymorphisms are associated with any particular disease or any particular response to therapy. Accordingly, it is maintained that the claimed invention lacks a specific and substantial utility and that the specification has not adequately taught one of skill in the art how to use the claimed invention.

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANT'S AMENDMENTS TO THE CLAIMS:

5. Claim 58 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

Claim 58 recites the limitation of detecting the presence of a polymorphism at position 12388 of SEQ ID NO: 5. While the specification as originally filed provides basis for the detection of a polymorphism at position 21388 of SEQ ID NO: 5, the specification does not provide basis for the detection of a polymorphism at position 12388 of SEQ ID NO: 5. This rejection may be

overcome by amendment of claim 58 to refer to nucleotide position "21388" in place of position "12388".

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (571) 272-0747. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (571)-272-0782.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Carla Myers
June 28, 2004

CARLA J. MYERS
PRIMARY EXAMINER